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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/769,686
	Filing Date	01/30/2004
	First Named Inventor	Lijun Xia
	Art Unit	1644
	Examiner Name	Michail Belyavskiy
Total Number of Pages in This Submission	Attorney Docket Number	5920.002

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation of POA, Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Certificate of Correction MAR 04 2008
Remarks 1. Transmittal (1 page); 2. Request For Certificate of Correction of Patent (2 pages); 3. Certificate of Correction (1 page); 4. Copy of Examiner's Amendment mailed 5/29/07 (6 pages); 5. Copy of AME & Response filed 2/12/2007 (9 pages); and 6. Postcard.		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	DUNLAP, CODDING & ROGERS, P.C.		
Signature			
Printed name	Christopher W. Corbett		
Date	02/28/2008	Reg. No.	36,109

CERTIFICATE OF TRANSMISSION/MAILING			
I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below: *** EXPRESS MAIL NO. EV 887845760 US DATED: 02/28/2008 ***			
Signature			
Typed or printed name	Christopher W. Corbett	Date	02/28/2008

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Express Mail: EV 887845760 US
Date Deposited: February 28, 2008

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.: 7,332,334 B2
Serial No.: 10/769,686
Issued: 02/19/2008
Inventor: Lijun Xia and Rodger P. McEver

Atty. Docket No.: 5920.002
Customer No.: 30589

Attn: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT
FOR PTO AND/OR APPLICANT'S MISTAKES (37 CFR 1.322(a) and 1.323)**

Enclosed are:

- ☐ PTO-2038 Credit Card Form;
- ☐ sb17 Fee Transmittal Form;
- ☒ sb21 Transmittal Form;
- ☒ 1 sheet(s) of form sb44 Certificate of Correction; and
- ☒ pre-addressed Postal Card

☒ PTO ERRORS

The exact column and line number where the mistakes occur in the patent as well as reference to the exact page and line number where the correct information occurs in the application file:

On the First Page: Delete the title "Hematopoietic Stem Cells Treated By In Vitro Fucosylation and Methods of Use" and replace with -- Fucosylated Hematopoietic Stem Cell Compositions --
(See Examiner's AME Mailed 5/29/07 & AME & Response, filed 2/12/2007, pg. 1)

In the Specification:

Column 1, line 1-3: Delete the title "Hematopoietic Stem Cells Treated By In Vitro Fucosylation and Methods of Use" and replace with -- Fucosylated Hematopoietic Stem Cell



Compositions -- .

(See Examiner's AME Mailed 5/29/07 & AME & Response, filed 2/12/2007, pg. 1)

Column 2, line 45: Delete "HSCS" and replace with -- HSCs -- .

(See Application filed 01/30/2004, pg. 5, line 1 of ¶ 6)

Column 8, line 53: Delete ".org/" and replace with -- .org/ -- .

(See Application filed 01/30/2004, pg. 19, line 7 of ¶ 33)

Column 9, line 66: Delete "Celigro" and replace with -- Cellgro) -- .

(See Application filed 01/30/2004, pg. 22, line 13 of ¶ 40)

Column 10, line 2: Delete "(MNCS)" and replace with -- (MNCs) -- .

(See Application filed 01/30/2004, pg. 23, line 1 of ¶ 40)

Column 14, line 14: After "leukemia" delete "(CML)," and replace with -- (JCML), -- .

(See Application filed 01/30/2004, pg. 33, line 4 of ¶ 73)

☒ [X] No fee is submitted herewith.

[] APPLICANT'S ERRORS

It is noted that errors appear in this patent of a clerical or typographical nature or a minor character as more fully described below. These errors occurred in good faith, and correction thereof does not involve such changes in the patent as would constitute new matter or would require re-examination. Thus, a Certificate of Correction is requested.

The exact column and line number where the mistakes occur in the patent are:

☐ [] Payment by credit card. Form PTO-2038 is attached..

[X] RETURN OF CERTIFICATE

Please send the Certificate of Correction to the undersigned.



Christopher W. Corbett, Reg. No. 36,109

DUNLAP CODDING & ROGERS, P.C.

P.O. Box 16370

Oklahoma City, Oklahoma 73113

Telephone: 405/607-8600

Facsimile: 405/607-8686

Agent for Applicant

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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 1 of 1

PATENT NO. : 7,332,334 B2
 APPLICATION NO.: 10/769,686
 ISSUE DATE : 02/19/2008
 INVENTOR(S) : Lijun Xia and Rodger P. McEver

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the First Page: Delete the title "Hematopoietic Stem Cells Treated By In Vitro Fucosylation and Methods of Use" and replace with – Fucosylated Hematopoietic Stem Cell Compositions – .

In the Specification:

Column 1, line 1-3: Delete the title "Hematopoietic Stem Cells Treated By In Vitro Fucosylation and Methods of Use" and replace with – Fucosylated Hematopoietic Stem Cell Compositions – .

Column 2, line 45: Delete "HSCS" and replace with – HSCs – .

Column 8, line 53: Delete ".orq/)" and replace with – .org/) – .

Column 9, line 66: Delete "Celigro)" and replace with – Cellgro) – .

Column 10, line 2: Delete "(MNCS)" and replace with – (MNCs) – .

Column 14, line 14: After "leukemia" delete "(CML)," and replace with – (JCML), – .

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Christopher W. Corbett, Reg. # 36,109
 Dunlap, Codding & Rogers, P.C.
 P.O. Box 16370
 Oklahoma City, OK 73113

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,686	01/30/2004	Lijun Xia	5920.002	9134
30589	7590	05/29/2007		
DUNLAP, CODDING & ROGERS P.C. PO BOX 16370 OKLAHOMA CITY, OK 73113				
			EXAMINER BELYAVSKIY, MICHAEL A	
			ART UNIT 1644	PAPER NUMBER
DATE MAILED: 05/29/2007				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 383 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 383 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

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Notice of Allowability

Application No.

10/769,686

Examiner

Michail A. Belyavskyi

Applicant(s)

XIA ET AL.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 02/12/07.
2. ☒ The allowed claim(s) is/are 14-19,22-41,55-60 and 63-91.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date 02/12/07
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413),
Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment.
8. ☒ Examiner's Statement of Reasons for Allowance.
9. ☐ Other _____.

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PATENT PROSECUTION

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Art Unit: 1644

DETAILED ACTION

1. Applicant's amendment, filed 02/12/07 is acknowledged.
2. Claims 14-19, 22-41, 55-60 and 63-91 are pending and allowed .

EXAMINER'S AMENDMENT

3. An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the Issue Fee.

4. Authorization for this Examiner's Amendment was given in a telephone interview with Christopher Corbett on 05/01/07.

In the Claims:

5. In claims 28, 29 and 30 second line, the phrase "fucosylated" has been replaced with -- said CD34⁺ CD38^{low/-} -- .
6. In claims 39, 40 and 41 second line, the phrase "fucosylated" has been replaced with -- said CD38^{low/-} -- .
7. In claims 69, 70 and 71 second line, the phrase "fucosylated" has been replaced with -- said -- .

REASONS FOR ALLOWANCE

8. The following is an Examiner's Statement of Reasons for Allowance:

The previous rejection of record, mailed on 12/22/06 is hereby withdrawn in view of:

- (i) The Examiner's Amendment set forth supra;
- (ii) Applicant's amendment filed 02/12/07.

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Art Unit: 1644

The prior art does not teach or suggest a composition of fucosylated HSC as recited in claims 14-19, 22-41, 55-60 and 63-91

9. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



MICHAEL BELYAVSKYI, PH.D.
PATENT EXAMINER

5/10/07

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Examiner-Initiated Interview Summary

Application No.

10/769,686

Applicant(s)

XIA ET AL.

Examiner

Michail A. Belyavskyi

Art Unit

1644

All Participants:(1) Michail A. Belyavskyi.(2) Christopher Corbett.**Status of Application:** _____

(3) _____.

(4) _____.

Date of Interview: 1 May 2007**Time:** _____**Type of Interview:**

- ☒ Telephonic
☐ Video Conference
☐ Personal (Copy given to: ☐ Applicant ☐ Applicant's representative)

Exhibit Shown or Demonstrated: ☐ Yes ☐ No

If Yes, provide a brief description:

Part I.

Rejection(s) discussed:

103

Claims discussed:

all

Prior art documents discussed:

Part II.

SUBSTANCE OF INTERVIEW DESCRIBING THE GENERAL NATURE OF WHAT WAS DISCUSSED:

*Applicant agreed the changes set forth in the Examiner's Amendment to put the case in condition for allowance.***Part III.**

- ☒ It is not necessary for applicant to provide a separate record of the substance of the interview, since the interview directly resulted in the allowance of the application. The examiner will provide a written summary of the substance of the interview in the Notice of Allowability.
- ☐ It is not necessary for applicant to provide a separate record of the substance of the interview, since the interview did not result in resolution of all issues. A brief summary by the examiner appears in Part II above.

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(Examiner/SPE Signature)

(Applicant/Applicant's Representative Signature – if appropriate)

Express Mail: EV 718813724 US
Date Deposited: February 12, 2007



Substitute for form 1449A/PTO

SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Complete if Known

Application Number	10/769,686
Filing Date	01/30/2004
First Named Inventor	Lijun Xia et al.
Group Art Unit	1645
Examiner Name	Michail A. Belyavskiy
Attorney Docket Number	5920.002

(use as many sheets as necessary)

U. S. PATENT DOCUMENTS

EXAM INIT.	Cite No. 1	U.S. PATENT NUMBER Number	Kind Code ² (If known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM- DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

EXAM INIT.	Cite No. 1	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Lines, Where Relevant Passages or Relevant Figures Appear	T ⁴
		Office 3	Number 4	Kind Code ⁵ (If known)				
HP			WO 2005/017115	A3	Mount Sinai Singal School of Medicine of New York University	02-24-2005		
HP			PCT/US04/06474		Search Report	12-05-2006		

U.S. and Foreign: ¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard St.3). ⁴Form Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard St. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

EXAM INIT.	PATENT DOCUMENTS	
	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	
Non Patent Documents: ¹ Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.		
Examiner Signature:		Date Considered: 05/07/07
EXAMINER: Initial if citation considered, whether or not citation is in conformance and not considered. Include copy of this form with next communication to applicant. **Place of Publication refers to name of publication in which the information was published.		

COPY

EXPRESS MAIL NO.: EV 718813724 US
Deposited On: February 12, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 10/769,686 Confirmation No.: 9134
Applicant(s) : Lijun Xia and Rodger P. McEver
Filed : 01/30/2004
TC/AU : 1645
Examiner : Michail A. Belyavskyi
Title : FUCOSYLATED HEMATOPOIETIC STEM CELL
COMPOSITIONS (AS AMENDED)
Docket No. : 5920.002
Customer No. : 30589

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE

Sir:

In response to the Official Action mailed December 22, 2006, please
amend the above-identified application as follows:

Amendment to the Title:

Please replace the title with:

"Fucosylated Hematopoietic Stem Cell Compositions"

Remarks/Arguments begin on page 2 of this paper.

REMARKS

This is intended to be a complete response to the official action mailed December 22, 2006, in which claims 14-19, 22-41, 55-60 and 63-91 were rejected in a new rejection under 35 U.S.C. § 103(a).

Rejection Under § 103(a)

Claims 14-19, 22-41, 55-60 and 63-91 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Hidalgo et al. (*J. Clin. Invest.*, 2002 Vol. 110, pages 559-569, IDS) in view of Kobzdej et al. (*Blood*, 2002, Vol. 100, pages 4485-4494 IDS).

In the rejection, it is stated:

"Hidalgo, et al., teach that homing of human HSCs comprising cells characterized as CD34⁺Cd38^{low/-} is impaired due to inability to bind with P-selectin or E-selectin (see entire document, Abstract in particular). Hidalgo, et al., further teach that said reduced ability to bind is due to a defect in the posttranslational processing of PSGL-1 protein that is expressed on the surface of said cells. Hidalgo, et al., further teach that said posttranslational modification is fucosylation and that forced fucosylation of said cells can be beneficial to improve homing of said cells. (see overlapping pages 568-569 in particular). Hidalgo et al., further teach that improving homing of said cells would have many implications for therapies using human progenitor/stem cells, for example for transplantation.

Hidalgo et al., do not explicitly teach a composition of fucosylated HSCs wherein fucosylated HSCs are produced by treating said cells in vitro with α 1,3 fucosyltransferase in the presence of a fucose donor (emphasis added).

Kobzdej et al., teach a method of forced fucosylation of intact WEHI-3 cells in vitro comprising treating said cells with α 1,3 fucosyltransferase in the presence of a fucose donor (see entire document, Abstract in particular). Kobzdej et al., teach that said

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treatment will result in fucosylation of said cells that would enhance their interaction with P-selectin or E-selectin."

Applicants respectfully traverse the rejection for the reasons provided below.

The Hidalgo et al. Reference

Regarding the teachings of Hidalgo et al., it is respectfully noted that several of the Examiner's assertions are incorrect.

Examiner asserts in the rejection, that:

"Hidalgo et al., further teach that said posttranslational modification is fucosylation and that forced fucosylation of said cells can be beneficial to improve homing of said cells." (see overlapping pages 568-569 in particular).

However, this is incorrect. Hidalgo et al. make absolutely no reference to "forced fucosylation" on pp. 568-569, or anywhere else in the article.

Furthermore, in the rejection, it is incorrectly stated that Hidalgo et al., teach that "reduced ability to bind is due to a defect in the posttranslational processing of PSGL-1 protein that is expressed on the surface of [CB-derived CD34⁺] cells" (emphasis added).

What Hidalgo et al. actually do state is:

"Our results suggest that the reduced interactions of CB-derived CD34⁺ cells are due to surface expression of nonfunctional PSGL-1." (p. 568, Col. 1, lines 26-29; emphasis added).

That is, Hidalgo et al. do not positively assert that the reason the non-binding subset of CD34⁺ cells fail to bind to P-selectin is definitely due to

surface expression of faulty PSGL-1; they only suggest it as the reason, and moreover, Hidalgo et al. further undermine confidence in their suggestion by stating:

"the molecular defect responsible for defective PSGL-1 function in the subset of CD-derived CD34+ cells remains to be defined" (p. 568, Col. 1, lines 31-33; emphasis added).

Hidalgo et al., do state that in mature leukocytes (not stem cells) posttranslational modifications in PSGL-1 include sialylation, fucosylation and tyrosine sulfation.

However, sialylation, fucosylation and tyrosine sulfation constitute completely separate and distinct enzymatic reactions. Moreover, sialylation and fucosylation are both dependent upon a number of other distinct glycosylation reactions which must occur before the sialylation, fucosylation and sulfation reactions can even be carried out in the cell (see below). Any of these reactions, if faulty, could affect posttranslational processing of PSGL-1. Hidalgo et al. merely identify a few of the many possible "posttranslational defects" which could occur, if indeed defective PSGL-1 was the cause of the impaired binding of the CD34⁺ cells to P-selectin.

Hidalgo et al. thus do not explicitly point to fucosylation as the defective step in the posttranslational processing of the defective CD34⁺ cells. Hidalgo et al. in fact give "equal" weight to sialylation, fucosylation and tyrosine sulfation as steps involved in posttranslational modification of PSGL-1 and

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provide absolutely no evidence that fucosylation in particular is deficient in the defective CD34⁺ cells.

The teachings of Hidalgo et al. provide at best an incomplete listing of several of the many steps involved in the posttranslational processing of the PSGL-1 polypeptide. It is well known in the art that there are numerous other glycosylation reactions which must occur even before sialylation and fucosylation, including for example, (1) linking a GalNAc (N-acetylgalactosamine) to an amino acid of the PSGL-1 polypeptide via N-acetylgalactosaminyltransferase; (2) linking a Gal (galactose) to the GalNAc via core1 β 1, 3 galactosyltransferase; (3) linking a GlcNAc (N-acetylglucosamine) to the GalNAc via an N-acetylglucosaminyltransferase, and (4) linking a Gal to the GlcNAc via β 1, 4 galactosaminyltransferase.

Hidalgo et al. identify none of these four crucial steps as potentially causative of the defective posttranslational processing, even though these steps must occur even before the sialylation and fucosylation steps noted by Hidalgo et al.

Most notably, Hidalgo et al. are silent as to which of the posttranslational processing steps is defective, only suggesting (literally) that the posttranslational defect may involve one of these three steps. Further, no data regarding defective fucosylation are provided. Hidalgo et al. thus provide no specific method of rectifying the unspecified defective posttranslational steps

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(since, contrary to Examiner's assertion, forced fucosylation is not suggested as a mitigating method) and, Hidalgo et al. most certainly provide no expectation of success of curing the posttranslational defect in the CD34⁺ cells.

As courts have repeatedly held, an "obvious-to-try" standard cannot be used to establish a prima facie case of obviousness. See, for example, *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988), or *In re Roemer*, 59 USPQ2d 1527 (Fed. Cir. 2001).

But, as is evident from the above, the teachings of Hidalgo et al. do not rise even to a level of "obvious-to-try" since there is no suggestion in Hidalgo et al. of how to correct the defective PSGL-1 on the CD34⁺ cells.

The Kobzdej et al. Reference

Now, even if, assuming arguendo, the teachings of Hidalgo et al. did suggest defective fucosylation (which they do not, as proven above), a person of ordinary skill in the art would not look to the secondary reference, Kobzdej et al., to modify the teachings of Hidalgo et al.

It is respectfully noted that the Examiner is completely incorrect in his assertion that Kobzdej et al. teach that "said treatment [by fucosylation] of said [CD34⁺] cells would enhance their interaction with P-selectin or E-selectin." In fact, Kobzdej et al. teach exactly the opposite.

In particular, Kobzdej et al., teach that:

- (1) "forced fucosylation of intact cells did not significantly augment their ability to bind to fluid-phase P- or E-selectin or

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to roll over immobilized P- or E-selectin under flow" (Abstract; emphasis added);

- (2) "Despite the large increase in sLe^x and Le^x epitopes, forced fucosylation with FTVI either failed to increase or only modestly increased binding of fluid-phase P-selectin or E-selectin to WEHI-3 cells or murine neutrophils (Figure 8)." (p. 4491, 1st complete paragraph of Col. 1; emphasis added);
- (3) "Control and FTVI-treated murine neutrophils also rolled similarly on P- and E-selectin (Figure 10A), resisted detachment from E-selectin equivalently as wall shear stress was increased (Figure 10B), and rolled with similar velocities on P- and E-selectin (Figure 10C-D). Thus, the FTVI-mediated addition of epitopes for sLe^x and Le^x to the surfaces of WEHI-3 cells or murine neutrophils did not significantly augment interactions with P- or E-selectin." (p. 4491, 1st and 2nd paragraphs of Col. 1; emphasis added);
- (4) "Forced fucosylation with an exogenous α 1-3-fucosyltransferase creates many sLe^x epitopes but does not substantially increase selectin ligands." (p. 4491, last complete sentence of Col. 2; emphasis added); and
- (5) "It is striking that addition of FTVI and GDP-fucose created many sLe^x epitopes but did not significantly increase selectin ligands" (p. 4492, last three complete sentences of Col. 3; emphasis added).

In view of the above, it is evident that Kobzdej et al. teach away from the present invention and thus are contrary to the examiner's assertion that it would be obvious to a person of ordinary skill in the art to modify the teachings of Hidalgo et al. with the teachings of Kobzdej et al. to treat the cells of Hidalgo et al. with α 1,3 fucosyltransferase even if Hidalgo et al. suggested forced fucosylation (which it does not).

The teachings of Kobzdej et al. clearly indicate that forced fucosylation does not enhance binding of murine neutrophils and WEHI-3 cells to P- or E-selectin (much less CD34⁺ cells or other stem cells). Kobzdej et al. thus in fact teach away from the present invention. It is well established that references which teach away from the invention are evidence of non-obviousness. A person of ordinary skill in the art, given an understanding of the Kobzdej et al. reference would not be motivated to use forced fucosylation to treat the CD34⁺ cells of Hidalgo et al., in fact, he would be motivated not to do so because Kobzdej et al. teach that there would be no reasonable expectation of success in doing so.

Clearly, given the teachings of Kobzdej et al., a person of ordinary skill in the art would reasonably expect that such fucosylated cells would not have enhanced binding to P- or E-selectin and thus would not be motivated to treat the cells in this manner and indeed would be motivated not to do so.

MPEP § 2143.02 indicates that "a reasonable expectation of success" is required for a determination of obviousness. Yet, as is clear from Kobzdej et al., there is no reasonable expectation of success in view of the contrary teachings that forced fucosylation does not enhance binding of cells to P-selectin or E-selectin, indeed, there would be an "expectation of failure".

In summary, (1) Hidalgo et al. do not demonstrate or state that the defective binding to P-selectin is due to errors in fucosylation of PSGL-1 protein

on CD34⁺ cells and do not teach that forced fucosylation of CD34⁺ cells can be beneficial in improving homing of such cells, and (2) Kobzdej et al. do not teach that forced fucosylation is effective in enhancing binding of murine cells (much less CD34⁺ stem cells) to P-selectin or E-selectin.

As described and explained above, neither the Hidalgo et al., nor Kobzdej et al. references, alone or together, support a conclusion of obviousness.

In view of the above, applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above, applicants submit the claims are now in condition for allowance and request issuance of a Notice of Allowance therefor.

Respectfully submitted,



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